

**Translation**

**PATENT COOPERATION TREATY**

**PCT**

**INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY**  
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference <b>R 03114</b>	<b>FOR FURTHER ACTION</b>	See Form PCT/IPEA/416
International application No. <b>PCT/FR2004/002021</b>	International filing date (day/month/year) <b>28.07.2004</b>	Priority date (day/month/year) <b>28.08.2003</b>
International Patent Classification (IPC) or national classification and IPC <b>C07B37/04, C07B43/06, C07D231/12</b>		
Applicant <b>RHODIA CHIMIE</b>		

1.	This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2.	This REPORT consists of a total of <u>5</u> sheets, including this cover sheet.
3.	This report is also accompanied by ANNEXES, comprising: a. <input type="checkbox"/> (sent to the applicant and to the International Bureau) a total of _____ sheets, as follows: <input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions). <input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box. b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4.	This report contains indications relating to the following items: <input checked="" type="checkbox"/> Box No. I Basis of the report <input type="checkbox"/> Box No. II Priority <input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability <input type="checkbox"/> Box No. IV Lack of unity of invention <input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement <input type="checkbox"/> Box No. VI Certain documents cited <input type="checkbox"/> Box No. VII Certain defects in the international application <input type="checkbox"/> Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/FR2004/002021

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

- ☐ This report is based on translations from the original language into the following language \_\_\_\_\_ which is the language of a translation furnished for the purposes of:
- ☐ international search (Rule 12.3 and 23.1(b))
  - ☐ publication of the international application (Rule 12.4)
  - ☐ international preliminary examination (Rule 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on (replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):

- ☐ the international application as originally filed/furnished

- ☒ the description:

pages 1-35 as originally filed/furnished

pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_

pages\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_

- ☒ the claims:

nos. \_\_\_\_\_ as originally filed/furnished

nos.\* \_\_\_\_\_ as amended (together with any statement) under Article 19

nos.\* 1-29 received by this Authority on 09.12.2004 with letter of 19.11.2004

nos.\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_

- ☐ the drawings:

sheets \_\_\_\_\_ as originally filed/furnished

sheets\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_

sheets\* \_\_\_\_\_ received by this Authority on \_\_\_\_\_

- ☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages \_\_\_\_\_

☐ the claims, nos. \_\_\_\_\_

☐ the drawings, sheets/figs \_\_\_\_\_

☐ the sequence listing (specify): \_\_\_\_\_

☐ any table(s) related to sequence listing (specify): \_\_\_\_\_

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages \_\_\_\_\_

☐ the claims, nos. \_\_\_\_\_

☐ the drawings, sheets/figs \_\_\_\_\_

☐ the sequence listing (specify): \_\_\_\_\_

☐ any table(s) related to sequence listing (specify): \_\_\_\_\_

\* If item 4 applies, some or all of those sheets may be marked "superseded."

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/FR2004/002021

**Box No. V** Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. Statement**

Novelty (N)	Claims <u>1-29</u>	YES
	Claims _____	NO
Inventive step (IS)	Claims _____	YES
	Claims <u>1-29</u>	NO
Industrial applicability (IA)	Claims <u>1-29</u>	YES
	Claims _____	NO

**2. Citations and explanations (Rule 70.7)**

1. The present application relates to a very general method for forming a C-C or C-het bond from an unsaturated compound having a leaving group and a nucleophilic compound in the presence of a copper-based catalyst, a base and a nitrile-type solvent and in the absence of a ligand.  
The examples only disclose the arylation of nucleophilic compounds (C and heteroatom).
2. At first sight, the prior art discloses only the use of a copper-based catalyst in the presence of a ligand, generally diamine or sometimes simply having a heteroatom (D1 to D4).
- 2.1 D1 discloses a method for forming a C-C or C-heteroatom bond, more particularly the arylation of pyrazole or acyclic nitrogen compounds (hydrazone...). Copper is used jointly with imine-type bidentate ligands. A certain number of solvents are tested and acetonitrile appears to be the most effective. The present application therefore differs from D1 only in the absence of ligand, whereas in D1 copper is associated with a ligand.
- 2.2 D4 discloses a method for arylating diethyl malonate in the presence of CuI + phenol ligand, of CsCO<sub>3</sub> in THF. A comparative test in the absence of a ligand is

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/FR2004/002021

Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
	<p>however mentioned; the yield is 80 % (a drop of 10 % relative to the test with the phenol ligand, see page 272, note (23)).</p> <p>Although the teaching of D4 may appear to dissuade a person skilled in the art from using a ligand, the yields obtained by the present application are nevertheless very much lower than those of D1 and are comparable or even lower than the 80 % yield obtained by D4 in the absence of a ligand.</p> <p>2.3 If the technical problem is considered to be that of obtaining the yields achieved by the present application, a person skilled in the art would have combined D1 with D4 without exercising inventive skill, given that such a person knows from D4 that the presence of a ligand is not compulsory for the reaction to work even if the yield achieved is lower than in D1 (80 %).</p> <p>The yields achieved by the present application are not surprising, given that they are clearly lower than those obtained in the presence of ligands (comparison with D1), a fact confirmed by D4.</p> <p>A person skilled in the art would have considered this alternative solution without exercising inventive skill.</p> <p>3. The same reasoning against an inventive step also applies when the comparative example of D4 is taken as the closest prior art, which differs only in the solvent used, given that D1 strongly encourages the use of nitrile solvent.</p> <p>4. D5 and D6 disclose the same reaction, in the absence of ligand and solvent, by microwave heating. The yields obtained are also in the 80 % range.</p> <p>5. Furthermore, the examples given by the applicant</p>

Box No. V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

appear to show that the substrate on which arylation should take place must have a group capable of acting as a ligand (phenol, pyrazole, diethylmalonate). In other words, the absence of ligand must in some way be compensated by the presence in the starting compound of heteroatoms capable of complexing with copper. However, the present application covers a far broader range of compounds and a doubt therefore arises as to whether the technical problem is effectively solved over the entire claimed range. For this reason also, the present application does not involve an inventive step (PCT Article 33(3)).

6. Finally, a person skilled in the art is well aware that nucleophile substitution reactions are highly dependent on numerous factors, such as the starting materials, the steric size thereof, the leaving groups, etc. However, the applicant takes a few specific examples, all of which relate to arylation based on benzene iodide or bromide, and generalises them to any kind of unsaturated substrate having a leaving group. The present Authority considers that such a generalisation lacks support (PCT Article 6) and therefore that the technical problem is not solved over the entire range claimed by the present application, which also results in a lack of inventive step (PCT Article 33(3)).
7. It is not currently possible to know which part of the application might be used as a basis for an acceptable new claim. However, if certain elements appear patentable to the applicant company, it is invited to justify this point of view, indicating in its reply any difference relative to the prior art and specifying the importance attributed thereto.